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(54) Title of invention: Gel-like composition

(57) Abstract

[Problem] To provide a gel-like composition containing a water soluble medicine such as lysozyme chloride, bromohexine hydrochloride or cynocobalamin, which is superior in preservative stability.

[Means for solving the problem] A gel-like composition containing a water soluble medicine, a vegetable polymer gelling agent, a sugar alcohol and water.

[Claim]

[Claim 1] A gel-like composition containing a water soluble medicine, a vegetable polymer gelling agent, a sugar alcohol and water.

[Claim 2] The gel-like composition according to claim 1 wherein solubility in water of the medicine is 1g/L or more at 25°C.

[Claim 3] The gel-like composition according to claim 1 or 2 wherein the medicine which has solubility in water of 1g/L or more at 25°C is lysozyme chloride, bromohexine hydrochloride or cynocobalamin.

[Claim 4] The gel-like composition according to claim 1 wherein the vegetable polymer gelling agent is one or more agents selected from carageenan, locust bean gum and xanthan gum.

[Claim 5] The gel-like composition according to claim 1 wherein the sugar alcohol is one or more selected from solbitol, maltitol, erythritol, mannitol, xylitol and trehalose.

[Detailed description of the invention]

[0001]

[Technical field]

The present invention relates to a gel-like composition, more in detail relates to a gel-like composition containing a water soluble medicine which is superior in preservative stability and can be easily orally taken.

[0002]

[Background art]

Medicines such as lysozyme chloride and bromohexine hydrochloride have been administered in granules, capsules, tablets and so on.

[0003]

However, these preparations are not easily orally taken for an aged person or a small child who is poor in swallowing (with dysphagia) and when a healthy adult takes them, water is necessary. Therefore, these preparations are not ones whenever and wherever they can be taken.

[0004]

[Problem to be solved by invention]

The present inventors have studied to prepare a gel-like preparation which is easily orally taken for an aged person or a small child who is poor in swallowing (with dysphagia), and the preparation does not need water even in case of taking orally.

However, when water soluble medicines such as bromohexine hydrochloride and so on is turned into gel, and thereto is admixed sucrose as a sweetener, the problem that the medicines are inactivated and its stability can not be retained occurs.

[0005]

Problem of the present invention is to provide a gel-like composition containing a water soluble medicine such as lysozyme chloride or bromohexine hydrochloride, which is superior in preservative stability.

[0006]

[Means for solving the problem]

The present inventors have been extensively studied and as a result have found that by adding a sugar alcohol instead of sucrose, water soluble medicines such as lysozyme chloride are stabilized in said gel. Namely the present invention relates to a gel-like composition containing a water soluble medicine, a vegetable polymer gelling agent, a sugar alcohol and water.

[0007]

[Embodiment for practicing the invention]

The water soluble medicines used in the present invention are ones which are soluble in water 1g/L or more at 25°C and are illustrated as lysozyme chloride, bromohexine hydrochloride, Vitamin B12 (e.g., cynocobalamin, hydroxocobalamin, mecobalamin, etc.). These medicines are used alone or in combination of them.

[0008]

The gelling agent used in the present invention is preferably a vegetable polymer gelling agent. In case of an animal polymer gelling agent, the preservative stability is not good and even when a sugar alcohol is used instead of sucrose, the stability of the medicine and gel is not retained.

[0009]

As vegetable polymer gelling agents are illustrated carageenan, locusto bean gum and xanthangum.

[0010]

With regard to the amount of the gelling agent, carageenan is 0.01 to 20 w/w% per composition, preferably 0.1 to 10w/w% from the view point of taking easiness and stability with time. Xanthangum is 0.01 to 5 w/w% per composition, preferably 0.1 to 0.6 w/w% from the view point of formulation of the preparation. Locust bean gum is 0.01 to 10 w/w% per composition, preferably 0.1 to 5 w/w% from the view point of stability with time.

[0011]

These gelling agents are contained alone or in combination of them, preferably a combination of carageenan, xanthangum and locust bean gum from the view point of formulation of the preparation and stability with time. The most preferable ratio by w/w of carageenan, xanthangum and locust bean gum is 0.5-2: 1 : 1.

[0012]

The sugar alcohol used in the present invention is mixed to the gel-like composition in order to give sweetness to take easily. As such sugar alcohols, are illustrated solbitol, maltitol, erythritol, mannitol, xylitol and trehalose.

[0013]

The amount of a sugar alcohol is 0.5 to 65w/w% per composition, preferably 3 to 40w/w% from the view point of taking easiness. The sugar alcohols may be

contained alone or a combination of them.

[0014]

Water used in the present invention is essential to make a gel and the amount of water is varied with a kind of other ingredients or intended gel strength, but 10 to 99w/w% per composition. When water is less than 10w/w%, the preparation does not compose a gel suitable for taking it.

[0015]

Furthermore, the gel-like composition of the present invention can contain pharmaceutically acceptable excipients (e.g. a sweetener, a flavoring substance, a perfume, a stabilizer, a filler or a preservative) in the amount as long as not destroying the stability of the gel or the medicine. For example, a sweetener such as stevioside or thaumatin; a flavoring substance such as citric acid or cocoa powder; a suface active agent such as polyoxyethylene hydrogenated castor oil or polyoxyethylene sorbitan fatty acid ester; a preservative such as methylparaben, ethylparaben, propylparaben or butylparaben; a stabilizer such as EDTA, erythorbic acid or BHT (dibutyl hydroxytoluene); and a filler such as light silicic anhydride.

[0016]

The gel-like composition of the present invention can be prepared by a conventional method adapted in a gel-formation field like this. For example, a water soluble medicine, a vegetable polymer gelling agent, a sugar alcohol such as maltitol and so on are mixed with other excipients, and then the mixture is dispersed in desired amount of water and dissolved under heating. The solution is poured in a desired sized and formed vessel suitable for taking easily and is solidified under cooling to prepare the gel-like composition.

[0017]

[Effect of invention]

It has become possible to provide a stable gel-like composition containing a water soluble medicine such as lysozyme chloride, bromohexine hydrochloride, cynocobalamin, hydroxocobalamin, mecobalamin, etc. according to the present invention.

[0018]

[Example]

The present invention is more in detail explained by Examples, Comparative examples and Tests.

[0019]

Example 1

Sodium citrate 0.4g, citric acid 0.1g, carageenan 1g, locust bean gum 0.5g, xanthangum 0.5g, propylparaben 0.02, and calcium lactate 0.5g were mixed with sorbitol 25g, and the mixture was added to water 41.88g. After the mixture was stirred for more than 30 min. at room temperature, the mixture was heated at more than 60°C to dissolve to get solution A.

[0020]

Then lysozyme chloride 6g was dissolved in water 30g and the solution was heated at 50 to 60°C to get solution B.

[0021]

Solution A and solution B were mixed under reduced pressure (in order to remove bubbles) while keeping at 50 to 60°C. The mixture was poured to 10mm of its depth of a pillar-like vessel (diameter: 3mm, depth: 12mm). The mixture in the vessel was cooled at less than 30°C to solidify to prepare an objective gel-like composition.

[0022]

Example 2

According to the method of example 1 was prepared Gel having the ingredients described in following table 1.

[0023]

Example 3

According to the method of example 1 was prepared Gel having the ingredients described in following table 1.

[0024]

Example 4

According to the method of example 1 was prepared Gel having the ingredients described in following table 1.

[0025]

Example 5

According to the method of example 1 was prepared Gel having the ingredients described in following table 1.

[0026]

Comparative example 1

According to the method of example 1 was prepared Gel having the ingredients

described in following table 1.

[0027]

[Table 1]

Ingredient	Example 1	Example 2	Example 3	Example 4	Example 5	Comparative example 1
Carageenan	1.0g	2.0g	0.2g	0.2g	0.2g	0.2g
Xanthangum	0.5g	0.1g	0.5g	0.5g	0.5g	0.5g
Locust bean gum	0.5g	1.0g	0.5g	0.5g	0.5g	0.5g
Calcium lactate	0.5g	0.2g	0.01g	0.01g	0.01g	0.01g
Citric acid	0.1g	0.1g	0.1g	0.1g	0.1g	0.1g
Sodium citrate	0.4g	0.4g	0.4g	0.4g	0.4g	0.4g
Propylparaben	0.02g	0.02g	0.02g	0.02g	0.02g	0.02g
Lysozyme chloride	5.0g					
Bromohexine hydrochloride		1.2g				
Cyanocobalamin			0.15g			0.15g
Hydroxocobalamin				0.15g		
Mecobalamin					0.15g	
Sorbitol		5.0g	10.0g	10.0g	10.0g	
Multitol		5.0g	15.0g	15.0g	15.0g	
Erythritol	15.0g	5.0g				
Treharose	10.0g	5.0g				
Sucrose						25.0g
Purified water	Total 100g	Total 100g	Total 100g	Total 100g	Total 100g	Total 100g

[0028]

Test

Gels prepared by Examples 1 to 5 could be orally taken without water.

[0029]

The stability and so on were tested on Gels prepared by Examples and comparative example. The results were shown in table 2.

[0030]

The amount of active ingredients was measured by HPLC and so on.

[0031]

[Table 2]

	Example 1	Example 2	Example 3	Example 4	Example 5	Comparative example 1
Condition for preservation	40°C-6 month	40°C-6 month	40°C-6 month	40°C-6 month	40°C-6 month	40°C-6 month
Colour	No change	No change	No change	No change	No change	No change
Smell	Almost nothing	Almost nothing	Almost nothing	Almost nothing	Almost nothing	Almost nothing
Syneresis	Almost nothing	Almost nothing	Almost nothing	Almost nothing	Almost nothing	Almost nothing
Taking easiness	No change	No change	No change	No change	No change	No change
Content of active ingredient	◎	○	○	○	○	X

◎: Lowering rate comparing with the amount just after preparing is less than 10%.

○: Lowering rate comparing with the amount just after preparing is 10% to 30%.

X: Lowering rate comparing with the amount just after preparing is more than 30%.